

**REMARKS**

Claim 32 has been amended as discussed at the interview to replace “analyzing” with “detecting” and this is understood to distinguish both Crooke and unspecified art related to antisense concepts apparently known to the Office. Claim 32 has also been amended for clarification to verify that the requirement of the preamble is a feature of the substantive steps carried out in the claim. The nature of the extract prepared must be from an organism in which it is suspected that PTGS is occurring, in view of the requirement of the preamble that the method is to detect PTGS in an organism. The requirement of determining sequence identity or similarity with a target gene as opposed simply to determining identity or similarity with the target gene has been moved to dependent claim 66, so that claim 41 may properly depend from claim 32. None of this is new matter and entry of amendment to claim 32 is respectfully requested.

In addition, claim 41 has been amended to conform more closely with the description of probing a library in the specification. On page 6 of the specification, the first full paragraph contains a paraphrase of claim 41 as now proposed.

This amendment also therefore does not constitute new matter and more closely corresponds to the specification than the previous wording.

**Restriction and Election of Species**

Claims 33, 34, 39 and 40 were withdrawn as directed to non-elected species. Going back to the restriction requirement, applicants note that these claims were all included in Group I and thus the withdrawn claims are directed to, as the Office states, a non-elected species, not a non-elected

invention. Since non-elected species are subject to inclusion within the examination should a linking claim be allowed, retention of these claims in the application is believed proper.

#### Priority

Applicants appreciate the accordation of priority as claimed to U.S. 09/491,549 filed 26 January 2000 and to the GB application from which priority is claimed, GB99/25459.1 filed 27 October 1999. Applicants understand that claim 41 is granted the benefit only to 26 January 2000. It is assumed that this is because a similar claim appears in the '549 application whereas the specification discusses these steps in conjunction with plants. The only difference between the application filed 26 January 2000 and that filed 27 October 1999 is that the later-filed application contains claims and the earlier-filed application does not. The specifications are identical. In any case, the matter is academic with respect to the rejection under § 102(e) set forth in this Office action, since, as is shown below, that rejection is not correct.

#### Previous Rejections Over the Art and Under 35 U.S.C. § 112

Applicants greatly appreciate the withdrawal of these rejections.

#### The Rejection for Anticipation

There is only one outstanding basis for rejection remaining, that of all examined claims under 35 U.S.C. § 102(e) over Croke (U.S. 6,107,094) as evidenced by Claycomb and Lanson (*Biochem. J.* (1987)).

Claycomb and Lanson is cited, apparently, only for its disclosure that *c-raf* is a proto-oncogene in mammals. This point is certainly conceded. Table 1 of Crooke clearly labels the dsRNA shown as SEQ ID NO:1 and SEQ ID NO:2 as *c-raf* targeted sense/antisense oligonucleotides. This simply shows that the double-stranded RNA in Table 1 of Crooke has sequence identity or similarity with a portion of a mammalian gene.

The real question, then, is whether the methods described by Crooke in columns 50-51 which utilize double-stranded RNA anticipate the method as claimed. From a review of these columns, applicants assume that the Examiner intends Example 27-a to be that to be compared to the method of the invention. Example 26 is directed to determining the nature of 5' termini left by nuclease cleavage and Example 27-b is directed to purification of the relevant enzymes (dsRNases) themselves.

First, the method of the invention is to detect PTGS of a target gene in an organism, and Example 27-a clearly does not accomplish this. Example 27-a is directed to a method to assess whether double-stranded RNases are present in an extract.

No doubt the Office assumes that the preamble is irrelevant to claim interpretation. However, this is not true when the preamble determines the nature of the body of the claim. This was illustrated, for example, in *Corning Glass Works v. Sumitomo Electric U.S.A., Inc.*, 868 F2d 1251, 9 USPQ2d 1962 (Fed. Cir. 1989) where claims were directed to a waveguide and the structural features in the body of the claim seemed to read on an unrelated apparatus. In that case, the Court held that the limitations of the preamble needed to be read into the structural features of the claim because the fact that the claimed apparatus was a waveguide inherently imposed structural characteristics on those explicitly set forth.

In the present case, the structural characteristic imposed on the substrate used in the claimed method has now been explicitly introduced into the claim by amendment. Thus, there is no question that the extract that is the subject of the first step must have been extracted from an organism in which it is suspected that PTGS is occurring. There is no reason to assume that the liver cytosolic and nuclear extracts of Crooke are prepared from such an organism.

Second, step 1 in claim 32 as amended also requires detecting the presence as opposed to the absence of SRMs that are 20-30 nucleotides in length in the extract. It does not appear that that is what is being detected in Example 27-a. It appears that the much shorter cleavage products of the supplied double-stranded RNA are the subject of detection.

The third step, which requires characterizing any SRMs to determine identity or similarity with a target gene is not done either. At best, the procedure in Example 27-a analyses the RNA in the extract for length alone, and not for identity or similarity to a target gene the silencing of which is to be determined.

As applicants are certain the Office is aware, in order for anticipation to be found, each and every limitation of the claim must be found explicitly or inherently in a single prior art document. This is far from the case here. The claimed method bears almost no resemblance to Example 27-a or any other procedure set forth in Crooke that applicants are able to find. Thus, this rejection may be withdrawn as to claim 32, and therefore as to all examined claims.

Although this should settle the matter, for completeness, applicants point out that in claim 41 it is also necessary to probe a library of genes from the organism and to identify the genes from the library that bind to any SRMs present in the extract. Respectfully, applicants are unable to find any step of probing a library of genes from any organism in Example 27-a. The Office simply

states that the nuclear extract contains a library of rat genes. While it is not contested that the nuclear extract may well have contained rat chromosomal material, to assert that this means the extract contains a “library” of rat genes would be stretching the meaning of the term “library” out of the context of claim 41 which clearly requires that the library be prepared in such a way that the sequences of the extracted SRMs can be used to probe the genes in the library. In any event, there is no probing of any library done in Crooke.

Similarly, claim 66 requires determining sequence identity or similarity with a target gene, a step that is nowhere to be found in Crooke.

With respect to claim 49, the reference to column 14, line 15, is not apposite because this refers not to RNA that might be recovered from an extract, but rather to the prepared oligonucleotides of the invention disclosed in Crooke.

### Conclusion

Claim 32 and its dependent claims are neither anticipated nor even suggested by Crooke. Therefore, the examined claims are in a position for allowance. Applicants very much appreciate the recognition that the claims, as amended, are free of Crooke and other unidentified art perhaps not cited in the original rejection. Again, the helpful discussion at the interview is very much appreciated.

Since claim 32 is a generic claim which covers the subject matter of claims 33-34 and 39-40, these claims may be rejoined and allowed as well. Therefore, applicants respectfully request that claims 32-37, 39-41, 49 and 66 be passed to issue.

